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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,980	10/02/2003	Ghislaine Mayer	NIH209.001C1	1240

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/677,980	MAYER ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *11-19,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/27/05&11/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response and amendment

1. Applicant's response to restriction and amendment filed on 11/09/05 is acknowledged. Applicants elected Group I, claims 1-10 and 20-21 for prosecution in this application.

Status of claims

2. Claims 1-23 are pending

Claims 1-19 have been amended.

Claims 1-10 and 20-21 are under investigation. There is no species election required in the elected invention. The examiner regrets the oversight made in the restriction.

Claims 11-19 and 22-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Priority

3. This application 10/677,980, 10/02/2003 is a CON of PCT/US02/10071 03/29/2002 which claims benefit of 60/281,130 04/02/2001.

Information Disclosure Statement

4. Information Disclosure Statements (IDS) filed on 5/27/04 and 11/09/05 are reviewed and a signed copy of each is attached to this Office action.

Drawings

5. The drawings filed on 10/2/03 are acknowledged by the examiner.

Claim Rejections - 35 USC 112, first Paragraph

6. The following is a quotation of the first Paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying

7. Claims 1-10 and 20-21 are rejected under 35 U.5.C. 112, first Paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a composition and a method of vaccinating a human comprising a polypeptide, wherein the polypeptide comprises an amino acid sequence that encodes a BAEBL polypeptide or portion thereof, said polypeptide portion having consecutive amino acids taken from said BAEBL polypeptide or portion thereof, said portion is an amino acid sequence BAEBL region II having number of or portion thereof, wherein said BAEBL polypeptide or portion thereof is defined as having the amino acid sequence of SEQ ID NO: 2 or portion thereof wherein said BAEBL polypeptide or portion thereof is defined as having at least 70%, 80%, 90%, 95%, or 99% identity to the amino acid sequence of SEQ ID NO: 2 or portion thereof. Said BAEBL polypeptide or portion thereof is encoded by a polynucleotide, said BAEBL polypeptide or portion thereof has a polymorphism, said composition comprising an adjuvant.

Recitation of "a polypeptide or a polypeptide encoded by a polynucleic acid is interpreted as a polypeptide which comprises a part of SEQ.ID.NO: 2.

The specification describes as part of the invention, an isolated recombinant protein comprising the amino acid sequence SEQ.ID.NO: 2 encoded by DNA comprising the nucleic acid sequence, SEQ.ID.NO: 1 from *Plasmodium falciparum* merozoite. The specification teaches that this full-length protein contains 1210 amino acids and specifically binds to erythrocytes that lack glycophorin A. This protein is a sialoglycoprotein. SEQ.ID.NO: 2 and has reduced binding activity to Gerbich erythrocytes. However, the specification fails to disclose polypeptide of SEQ.ID.NO: 2 or portion having at least 70%, 80%, 90%, 95%, or 99% identity to the amino acid sequence of SEQ ID NO: 2.

Applicants broadly describe the invention as embracing any deletion by use of language in which a specified percent identity to amino acids SEQ.ID.NO: 2 can be changed in the protein encoded by SEQ.ID.NO: 1 (the examiner considers all these as variants of SEQ.ID.NO: 2 and

here after will be referred as variants of SEQ.ID.NO: 2. USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116). Therefore, a composition comprising the *Plasmodium falciparum* recombinant protein as set forth iSEQ.ID.NO: 2 and an adjuvant meets the written description provision of 35 U.S.C. 112, first Paragraph for the reasons set forth below:

The specification fails to teach variants of SEQ.ID.NO: 2 that can bind to erythrocytes that lack glycophorin A and is noted that the claimed variants do not exist as an invention independent of their function (examiner is considering them as variants and hereafter referred as variants of SEQ.ID.NO: 2). The actual relevant identifying characteristics of claimed variants having the claimed property (binding to erythrocytes that lack glycophorin A etc) of the protein can only be determined empirically by actually making recited variant and testing it to determine whether such a variant having the particularly disclosed properties of binding to erythrocytes that lack glycophorin A. For example, if there is a well-established correlation between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function. This specification does not teach such, and the art is devoid of this correlation for claimed variants. There is no written description support for variants of SEQ.ID.NO: 2 as claimed. In addition, a polypeptide comprising (open language) SEQ.ID.NO: 2 plus unlimited and unknown amino acids would result in an unknown protein without sufficient structure and completely lacking identifying characteristics such as function, i.e. bind to erythrocytes that lack glycophorin A. The specification fails to disclose any deletion

or change in an amino acid sequence, SEQ.ID.NO: 2 to obtain said variants that could be used in a composition or in the claimed method. The specification does not describe any use of said variant as claimed (comprising, open language) in identifying *Plasmodium* and do not meet the written description provision of 35 U.S.C. 112, first Paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116). See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016.

8. Claims 1-10 and 20-21 are rejected under 35 U.5.C. 112, first Paragraph, because the specification, while being enabling for a composition comprising the *Plasmodium falciparum recombinant* polypeptide BAEBL as set forth in the amino acid sequence SEQ.ID.NO: 2 or recombinant polypeptide encoded by the nucleic acid sequence SEQ.ID.NO: 1 and an adjuvant, does not reasonably provide enablement a composition and a method of vaccinating a human comprising a polypeptide, wherein the polypeptide comprises an amino acid sequence that encodes a BAEBL polypeptide or portion thereof, said polypeptide portion having consecutive amino acids taken from said BAEBL polypeptide or portion thereof, said portion is an amino acid sequence BAEBL region II having number of or portion thereof, wherein said BAEBL polypeptide or portion thereof is defined as having the amino acid sequence of SEQ ID NO: 2 or portion thereof wherein said BAEBL polypeptide or portion thereof is defined as having at least 70%, 80%, 90%, 95%, or 99% identity to the amino acid sequence of SEQ ID NO: 2 or portion thereof. Said BAEBL polypeptide or portion thereof is encoded by a polynucleotide and

adjuvant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly, connected, to make and use the invention commensurate in scope with these claims.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is preparing a recombinant protein, SEQ.ID.NO: 2 from merozoites of *Plasmodium falciparum.* The specification teaches the claimed recombinant protein contains 1210 amino acids and binds specifically to erythrocytes that lack glycophorin A and appears to be different from that of EBA-175 protein. The specification fails to provide an enabling disclosure other than the composition comprising the isolated recombinant protein comprising the amino acid sequence SEQ ID NO: 2 because it fails to provide any guidance regarding how to make and use variants either in a composition or in a method as claimed.

The state of the art is devoid of teaching variants of SEQ.ID.NO: 2. The current specification indicate that the claimed recombinant protein specifically binds to erythrocytes that lack glycophorin A, having different RBC specificities (example 2) for example reduced binding activity with Gerbich erythrocytes. The specification does not disclose that the claimed variants bind to glycophorin negative RBC. As taught by the prior art it is apparent that binding of Parasite ligand to erythrocyte receptor is a prerequisite to invasion of erythrocytes by the Parasite (Mayer et al PNAS2004, 101:2518-2523). Therefore, variants of the SEQ.ID.NO: 2

having no specific ligand must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis. Therefore, its use in a method or composition for preventing *Plasmodium* would require undue experimentation to practice as claimed. The specification provides no disclosure how to vaccinate human against Plasmodium (i.e., various species) using the claimed composition because it fails to provide guidance whether the claimed composition provides protection against *Plasmodium vivax, P. malariae* etc as each species *of Plasmodium* uses specific receptor in invading erythrocytes (see specification pages 1-2). Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Claim Rejections - 35 USC 112, second Paragraph

9. The following is a quotation of the second Paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-10 and 20-21 are rejected under 35 U.S.C. 112, second Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The abbreviation " BAEBL " is used without definition upon their first appearance in the claim 1.

Claim 1 is rejected as being vague for the recitation of " an amino acid sequence that encodes a BAEBL polypeptide or portion thereof". Generally nucleic acid sequence encodes the polypeptide.

Claim 3 is rejected as being vague for the recitation of "polypeptide portion---- consecutive amino acids 6, 7 --- etc" because there is no amino acid sequence identification

number is given to the BAEBL polypeptide. Therefore, it is unclear what are those consecutive amino acids.

Claim 8 is rejected as being vague for the recitation of " I at position 185, N at position 239, T at position 261, R at position 261, and E at position 285" because there is no amino acid sequence identification number is given to the BAEBL polypeptide.

Claim 20 recites the limitation "vaccine" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate Paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 12 2(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-10 and 20-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Narum et al US 20020127241 A1

Claims are drawn to a composition comprising a polypeptide and wherein the polypeptide comprises an amino acid sequence that encodes a BAEBL polypeptide or portion thereof, wherein the polypeptide portion is an amino acid sequence that encodes a BAEBL region II or portion thereof, said polypeptide portion is selected from the group consisting of an amino acid sequence having the following number of consecutive amino acids taken from said BAEBL polypeptide: 6 ------ 584, said BAEBL polypeptide or portion thereof is defined as having the amino acid sequence of SEQ ID NO: 2 or portion thereof and is defined as having at least 70%,

polypeptide: 6 ------ 584, said BAEBL polypeptide or portion thereof is defined as having the amino acid sequence of SEQ ID NO: 2 or portion thereof and is defined as having at least 70%, 80%, 90%, 95%, or 99% identity to the amino acid sequence of SEQ ID NO: 2 or portion thereof or open reading frame of SEQ ID NO: 1 or portion thereof, said BAEBL polypeptide or portion thereof is encoded by a polynucleotide which hybridizes to a second polynucleotide having the polynucleotide sequence of SEQ ID NO 1, said polypeptide has a polymorphism selected from the group consisting of I at position 185 etc, said second polypeptide comprises an amino acid sequence that encodes at least a portion of a Duffy binding protein or erythrocyte binding antigen-175 (EBA-175) of a malaria *Plasmodium* Parasite. Claims are also drawn to a method of vaccinating a human against a malaria Plasmodium Parasite comprising the step of administering said above vaccine composition wherein said step of administration is by protein immunization.

Narum et al disclose a composition comprising *P. falciparum* erythrocyte binding protein EBP2 (also known as paralogue of EBP-175, see abstract, Para # 0118,). The ebp2 gene encodes the ligand-binding domain RII (see FIG. 2 and summary of the invention, Para# 0010-0016,) The ORF of the partial gene sequence of ebp2 (Para # 0105, figure 2 and figure 1) encoded approximately 133-kDa protein. The molecular mass of EBP2 identified by immunoprecipitation was approximately130 –140kD (Example 2-5), which suggests that the protein comprises approximately 1200 amino acid sequence (see the sequence alignment) including 6-584 consecutive amino acids. . Therefore, it reads on claims 1-4. Further the same EBP2 polypeptide reads on the claimed BAEBL comprising the amino acid sequence SEQ.ID.NO: 2 as EBP2 is almost identical (with three conservative amino acids, see the sequence alignment) with claimed polypeptide and is encoded by polynucleotide sequence as shown in figure 2 and thus meets the claim limitations of 4-6. In the absence of evidence to the

contrary the reverse strand DNA hybridizes to the claimed SEQ.ID.NO: 1 since the disclosed protein encoded by nucleic acid is identical to the claimed. Therefore it meets the limitations of claim 7. The disclosed EBP2 polypeptide contains I at position 181 (please note applicants sequence contains I at position 181 not at 185 as claimed in claim 8 and therefore, the examiner considers this as a typographical error). Since EBP2 RII anti- recognized 3D7 and FVO schizont infected erythrocytes and the IFA showed co localization of EBP2 and EBA175 (see Para #0118), it is apparent that the composition used to raise antisera contains EBP 175 as a second polypeptide as claimed in claim 10. The prior art discloses method of preventing Plasmodium falciparum (see abstract, claims, Para # 0015) using disclosed composition as discussed above. The disclosed composition has been used to raise antisera (example 3). Therefore, the composition appears to be the same as claimed composition. Since the Office does not have the facilities for examining and comparing applicants' **composition** with the **composition** of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Thus the prior art anticipated the claimed invention.

13. Claims 1-7 and 10 are rejected under 35 U.S.C. 102 (b) as being anticipated by Dolan et al 1990, Journal of Clinical investigation Inc. Vol: 86, 618-24 (see IDS 7/27/04, NO: 14).

Claims have been discussed supra.

Dolan et al disclose a composition comprising soluble proteins from culture supernatant and parasite infected cellular sonicates of *Plasmodium falciparum* clones Dd2, Dd2/NM1 and Dd2/NM2. This composition reads on the claimed composition (claims 1-3) because the composition comprises proteins ranging from 140kD-175 kD proteins and protein is made up of amino acids including the region II of BAEBL. It appears polypeptide 140 kD is similar to

the claimed polypeptide, SEQ.ID.NO: 2 (claims 4-5 comprising 1210 amino acids) because the protein is isolated from *Plasmodium falciparum* and having comparable protein 140 kD as molecular weight of each amino acid is approximately 110 Dalton and associated with other proteins including 175 kD (see figure 5A /B) as claimed in claims 4-5 and 10. Further, the disclosed polypeptide is encoded by polynucleic acid that hybridizes to DNA from clones Dd2, Dd2/NM1 and Dd2/NM2 (see figure 4) and thus it meets the limitations of claims 6- 7. The prior art anticipated the claimed invention.

Remarks

14. No claims are allowed.

Conclusion

15. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A

message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D

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